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| APPLICATION NO.             | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------------------|-------------|----------------------|---------------------|------------------|
| 10/782,943                  | 02/23/2004  | Janet Kay Robertson  | MAJ-101US           | 7667             |
| 23122                       | 7590        | 06/25/2007           | EXAMINER            |                  |
| RATNERPRESTIA               |             |                      | BEISNER, WILLIAM H  |                  |
| P O BOX 980                 |             |                      | ART UNIT            | PAPER NUMBER     |
| VALLEY FORGE, PA 19482-0980 |             |                      | 1744                |                  |
|                             |             |                      | MAIL DATE           | DELIVERY MODE    |
|                             |             |                      | 06/25/2007          | PAPER            |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

|                              |                                       |   |  |
|------------------------------|---------------------------------------|---|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/782,943  | <b>Applicant(s)</b><br>ROBERTSON, JANET KAY |  |
|                              | <b>Examiner</b><br>William H. Beisner | <b>Art Unit</b><br>1744                     |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-47 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-47 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 23 February 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |  |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                               | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                      | 5) <input type="checkbox"/> Notice of Informal Patent Application                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date ____ | 6) <input type="checkbox"/> Other: ____  |

**DETAILED ACTION**

***Claim Rejections - 35 USC § 102***

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1, 4-8, 10 and 17-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Nisch et al.(US 6,315,940).

With respect to claim 1, the reference of Nisch et al. discloses an apparatus (10 or 80) for the performing multiplexed patch clamping comprising: an insulating layer (16 or 91) having a plurality of orifices (20, 84) there through; at least one electrode (21 or 85) electrically connected with each orifice; and a substrate (15 or 90) supporting said insulating layer and said electrodes, wherein said insulating layer, said electrodes, and said substrate are transparent, iridium oxide which would be inherently transparent(See column 4, lines 33-40, and column 9, lines 4-9). If not, the device would not provide the required transparency for the disclosed microscopy techniques (See column 4, lines 33-40).

With respect to claim 4, the electrodes can be electrically isolated (See column 8, lines 18-23).

With respect to claim 5, a part of each electrode is electrically connected to an orifice (See Figures 1, 3 and 5).

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With respect to claims 6 and 7, each orifice is electrically connected to two electrodes (85 and 8), wherein one electrode is a measuring electrode and the other electrode is a stimulus electrode (See column 8, lines 6-9).

With respect to claim 8, the orifice can be coated with cell adhesion material (See column 4, lines 21-24 and column 9, lines 12-19).

With respect to claim 10, the device includes reference electrode (87).

With respect to claim 17, the electrodes (85) are sandwiched between the insulating layer (91) and substrate (90).

With respect to claims 18 and 19, the reference of Nisch et al. discloses the use of glass, plastics or silicon for the insulating layer and substrate (See column 4, lines 33-40).

With respect to claims 20 and 21, the reference of Nisch et al. discloses the use of a microfluidic channel (23) between the insulating layer (16) and substrate (15) (See Figure 1).

With respect to claim 22, the substrate (90) defines the bottom of a multi-well plate (See Figures 4 and 5).

### ***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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4. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35

U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 9 and 11-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nisch et al.(US 6,315,940).

The reference of Nisch et al. has been discussed above.

With respect to claim 9, while the reference of Nisch et al. discloses the use of adhesion proteins, the reference does not list the specific substances of claim 9.

However, the use of collagen and polylysine is notoriously well known in the art as a cell adhesion material.

As a result, it would have been obvious to one of ordinary skill in the art to determine the optimal adhesion material based on the specific material of the substrate and/or cell to be used while providing the required adhesion for monitoring the cell.

With respect to claims 11-16, while the reference discloses that the reference electrode is spaced from the bottom of the orifice and the surfaces spaced from the bottom of the orifice can be treated to prevent cell adhesion (See column 5, lines 3-5, and column 4, lines 15-24), the reference does not specifically disclose that the reference electrode is treated and/or sandwiched in the device.

However, in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art to treat the electrode surface and/or reposition the reference electrode within the device for the known and expected result of preventing the adhesion of cells thereon while maintaining the required function of the reference electrode in the monitoring system. The specific method employed to prevent the cells from adhering to the surface would have been well within the purview of one having ordinary skill in the art.

6. Claims 2, 23-26 and 28-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nisch et al.(US 6,315,940) in view of Wang et al.(US 2002/0182627).

The reference of Nisch et al. has been discussed above.

With respect to claim 23, while the reference of Nisch et al. discloses that the device is used for patch clamping and microscopy techniques (See column 2, lines 49-67, and column 4, lines 37-40), the reference does not disclose the resistance of the seal formed and/or the performance of a fluorescence assay.

The reference of Wang et al. discloses that it is conventional in the art of patch clamping a cell to combine the ion channel recording with fluorescence imaging (See paragraph [0370]). The reference also discloses that when contacting a cell with an opening with an electrode, such as in the reference of Nisch et al., a gigaohm seal is achieved (See paragraph [0423]).

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the device of the primary reference to perform both patch clamping and fluorescence imaging of cells as suggested by the reference of Wang et al.

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With respect to claim 24, the method would include a step of allowing the cells to attach to the bottom of orifice which is required in both the references of Nisch et al. and Wang et al.

With respect to claim 25, monitoring the response of the cells to test compounds is well known in the art and would have been obvious, if not inherent, in the disclosures of Nisch et al. and Wang et al.

With respect to claims 2 and 26, the reference of Nisch et al. does not specifically disclose the diameters of the orifices.

The reference of Wang et al. discloses that the use of orifice openings between 0.1-100microns is known in the art (See paragraph [00337]).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to determine the optimum orifice diameter based merely on the size of the cells to be monitored in the system while maintaining the efficiency of the monitoring device.

With respect to claim 28, the electrodes can be electrically isolated (See column 8, lines 18-23).

With respect to claim 29, a part of each electrode is electrically connected to an orifice (See Figures 1, 3 and 5).

With respect to claims 30 and 31, each orifice is electrically connected to two electrodes (85 and 8), wherein one electrode is a measuring electrode and the other electrode is a stimulus electrode (See column 8, lines 6-9).

With respect to claim 32, the orifice can be coated with cell adhesion material (See column 4, lines 21-24 and column 9, lines 12-19).

With respect to claim 33, while the reference of Nisch et al. discloses the use of adhesion proteins, the reference does not list the specific substances of claim 9.

However, the use of collagen and polylysine is notoriously well known in the art as a cell adhesion material.

As a result, it would have been obvious to one of ordinary skill in the art to determine the optimal adhesion material based on the specific material of the substrate and/or cell to be used while providing the required adhesion for monitoring the cell.

With respect to claim 34, the device includes reference electrode (87).

With respect to claims 35-40, while the reference discloses that the reference electrode is spaced from the bottom of the orifice and the surfaces spaced from the bottom of the orifice can be treated to prevent cell adhesion (See column 5, lines 3-5, and column 4, lines 15-24), the reference does not specifically disclose that the reference electrode is treated and/or sandwiched in the device.

However, in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art to treat the electrode surface and/or reposition the reference electrode within the device for the known and expected result of preventing the adhesion of cells thereon while maintaining the required function of the reference electrode in the monitoring system. The specific method employed to prevent the cells from adhering to the surface would have been well within the purview of one having ordinary skill in the art.

With respect to claim 41, the electrodes (85) are sandwiched between the insulating layer (91) and substrate (90).



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With respect to claims 42 and 43, the reference of Nisch et al. discloses the use of glass, plastics or silicon for the insulating layer and substrate (See column 4, lines 33-40).

With respect to claims 44 and 45, the reference of Nisch et al. discloses the use of a microfluidic channel (23) between the insulating layer (16) and substrate (15) (See Figure 1).

With respect to claim 46, the substrate (90) defines the bottom of a multi-well plate (See Figures 4 and 5).

7. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nisch et al.(US 6,315,940) in view of Albritton et al.(US 2004/0058423).

The reference of Nisch et al. has been discussed above.

Claim 3 differs by reciting that the electrode is made of ITO.

The reference of Albritton et al. discloses that it is known in the art to manufacture transparent electrodes from ITO (See paragraphs [0011] and [0056]).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to employ electrode material that art known in the art while providing the required transparency for the optical monitoring of the cells in the device.

8. Claims 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nisch et al.(US 6,315,940) in view of Wang et al.(US 2002/0182627) taken further in view of Albritton et al.(US 2004/0058423).

The combination of the references of Nisch et al. and Wang et al. has been discussed above.

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Claim 27 differs by reciting that the electrode is made of ITO.

The reference of Albritton et al. discloses that it is known in the art to manufacture transparent electrodes from ITO (See paragraphs [0011] and [0056]).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to employ electrode material that art known in the art while providing the required transparency for the optical monitoring of the cells in the device.

9. Claim 47 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nisch et al.(US 6,315,940) in view of Wang et al.(US 2002/0182627) taken further in view of Dodgson (WO 01/48474).

The combination of the references of Nisch et al. and Wang et al. has been discussed above.

Claim 47 differs by reciting that the method includes centrifuging the cell into the orifice.

The reference of Dodgson discloses that it is conventional in the art to position a cell within a monitoring device by using centrifugal force (See page 7, line 10).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to position the cells within the orifices of the device of the modified primary reference using a centrifuging step for the known and expected result of providing an art recognized practice for positioning cells within an orifice of a monitoring device.

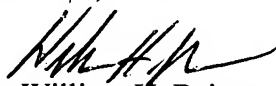
### ***Conclusion***

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10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to William H. Beisner whose telephone number is 571-272-1269. The examiner can normally be reached on Tues. to Fri. and alt. Mon. from 6:15am to 3:45pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gladys J. Corcoran can be reached on 571-272-1214. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

  
William H. Beisner  
Primary Examiner  
Art Unit 1744

WHB